

REMARKS

Claims 1-7, 10-54, and 57-79 are pending with claims 58 and 69-71 under consideration, claims 1-7, 10-54, 57, 69-68, and 72-79 having been withdrawn by the Examiner as drawn to non-elected subject matter. By the present communication, 58 has been amended and new claims 80-82 have been added. Upon entry of the present amendment, claims 58, 69-71, and 80-82 will be pending and under consideration. These amendments add no new matter as the claim language is fully supported by the specification and the claims as originally filed.

Information Disclosure Statement

The Office Action asserts that the Information Disclosure Statement filed on April 25, 2006 allegedly fails to comply with the requirements of 37 CFR 1.98(a)(2). In particular, the Action indicates that copies of the foreign documents listed were not provided. Pursuant to the Examiner's requirement, submitted herewith is a Supplemental Information Disclosure Statement, with accompanying Form 1449 listing all of the foreign patent documents, along with copies of the each of the cited documents. Consideration of all documents submitted to-date is respectfully requested.

Objections to the Specification/Abstract

The Examiner's objection to the abstract as allegedly not commencing on a separate sheet in accordance with 37 CFR 1.52(b)(4) is respectfully traversed. It is respectfully submitted that this objection is improper. Applicants respectfully direct the Examiner's attention to the MPEP at §608.01(b), ¶ 6.16.01 and "Examiner Note" number 3 that follows:

Abstract of the Disclosure: Placement

The abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text.

Examiner Note

3. This form paragraph should not be used during the national stage prosecution of international applications ("371 applications") if an abstract was published with the international application under PCT Article 21.

The present application is a US National Stage filing under 35 USC § 371 of International Application No. PCT/US04/18623. An abstract of the invention was published with the aforementioned international application. Thus, Applicants have met the requirements for an abstract of the disclosure. Accordingly, reconsideration and withdrawal are respectfully requested.

Nucleotide and/or Amino Acid Sequence Disclosure

The Examiner asserts that no sequence identifier is associated with the "consensus sequence" depicted in Figure 1B, nor is there a sequence identifier in the brief description of Figure 1B. The brief description of Figures 1A and 1B recites, "a consensus sequence for the last full repeat is set forth in Figure 1B (see, SEQ ID No. 49)." Moreover, a review of the Sequence Listing reveals that the consensus sequence (i.e., KLGXGLXFD/N) depicted in Figure 1B is identical to the sequence set forth in SEQ ID NO:49. It is therefore, respectfully submitted that the specification is in full compliance with 37 CFR §1.821-1.825. Accordingly, reconsideration and withdrawal of this objection are respectfully requested.

Objections to the Claims

The Examiner has objected to claim 58 for allegedly containing various informalities. Specifically, the Examiner asserts that claim 58 encompasses non-elected subject matter that includes various modifications to the third β -repeat of the fiber shaft. In efforts to reduce the issues and expedite prosecution, claim 58 has been re-written in independent form and does not include reference to modifications to the third repeat. Accordingly, reconsideration and withdrawal of this objection are respectfully requested.

The Examiner has further objected to claim 58 for reciting “modified fiber” rather than “modified fiber shaft.” Without acquiescing to the reasoning offered in the Action, claim 58 is amended herein to indicate that the modification is in the fiber shaft protein. Accordingly, reconsideration and withdrawal of this objection are respectfully requested.

Rejection under 35 U.S.C. §102(e)

Claims 58 and 69 stand rejected under 35 U.S.C. §102(e), as allegedly being anticipated by Vigne et al. (U.S. Patent No. 6,911,199). Applicants traverse the rejection as applied to the amended claims, for at least the reasons given below.

The Office Action alleges, in pertinent part, that Vigne teaches “targeted adenovirus vectors for delivery of heterologous genes, wherein modifications of the internal sites of the adenovirus fiber protein that include short targeting peptides fused to the C-terminus of the fiber protein, or the fiber HI loop (knob) target the modified adenoparticles to specific cell types,” citing the title and abstract (Office Action at p. 5). The Action further alleges that Vigne teaches that the fiber protein may be modified to have a shorter shaft or may be replaced with the shaft of another serotype. However, Vigne does not teach or suggest a modified adenovirus fiber in which the modification is in the last full repeat, wherein binding of the modified fiber to CAR is reduced.

Indeed, claim 58 expressly recites that “the modification is a mutation, insertion or replacement of at least one amino acid in a fiber shaft β -repeat corresponding to the last full β repeat, whereby binding of the fiber or of a viral particle containing such fiber to the Coxsackie-Adenovirus Receptor (CAR) is reduced compared to the unmodified fiber.” Such a modification of the last full repeat is not taught by Vigne. Rather, Vigne teaches large deletions or substitutions involving all or most of the shaft protein. Specifically, Vigne teaches modified Ad5 fibers in which large portions of the fiber shaft (*i.e.*, repeats 4-16 or repeats 4-19) are deleted, but the native last full repeat is left intact. Alternatively, Vigne teaches a substitution of the entire Ad5 fiber shaft with the fiber shaft of Ad3. Vigne is, however, silent with regard to a modification of the last full repeat as required by the present claims.

As stated in Hybritech Inc. v. Monoclonal Antibody, Inc., 231 U.S.P.Q. 81 (Fed. Cir. 1986), "It is axiomatic that for prior art to anticipate under 102 it has to meet every element of the claimed invention."

Therefore, because the instant claims recite an element which is not taught or suggested in Vigne, the reference does not anticipate the claimed invention.

Failure of the prior art to meet every element of the claimed invention does not meet the standard under §102. For these reasons, Applicants respectfully request that the rejection be withdrawn.

IV. Rejection under 35 U.S.C. §103(a)

Claims 58 and 69-71 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Vigne *et al.*, (supra) in view of Wickham *et al.* (US Patent No. 6,455,314). Applicants traverse the rejection as it applies to the pending claims, for at least the reasons given below.

The Office Action alleges that that Vigne teaches "targeted adenovirus vectors for delivery of heterologous genes, wherein modifications of the internal sites of the adenovirus fiber protein that include short targeting peptides fused to the C-terminus of the fiber protein, or the fiber HI loop (knob) target the modified adenoparticles to specific cell types," citing the title and abstract (Office Action at p. 5). The Action further alleges that Vigne teaches that the fiber protein may be modified to have a shorter shaft or may be replaced with the shaft of another serotype, but acknowledges that Vigne does not specifically describe fiber knot modifications confined to the AB or CD loop. The Action then supplies Wickham in an attempt to cure the deficiencies identified in the primary reference. However, Applicants respectfully submit that the references alone or in combination do not teach all of the elements of the present claims. It is further submitted the references provide no motivation to combine nor would the skilled artisan have had a reasonable expectation of success in achieving an adenovirus particle of the present claims because Vigne teaches away from adenovirus particles having the recited fiber shaft modification.

It is respectfully submitted the Examiner has not met the standard under 35 U.S.C. §103 for establishing a *prima facie* case of obviousness because cited art does not teach all of the elements of the present claims. As discussed above, claim 58 expressly recites that “the modification is a mutation, insertion or replacement of at least one amino acid in a fiber shaft β -repeat corresponding to the last full β repeat, whereby binding of the fiber or of a viral particle containing such fiber to the Coxsackie-Adenovirus Receptor (CAR) is reduced compared to the unmodified fiber.” Such a modification of the last full repeat is not taught by Vigne. Wickham cannot cure this deficiency because Wickham is silent with regard to modifications to the last full repeat of the fiber shaft protein.

Moreover, it is respectfully submitted that Vigne teaches away from the adenovirus particles of the present claims. The M.P.E.P. at §2146(X)(D)(2), states that it “is improper to combine references where the references teach away from their combination,” citing *In re Grasselli*, 713 F.2d 731, 743, 218 USPQ 769, 779 (Fed. Cir. 1983). According to the Federal Circuit, “[a] *prima facie* case of obviousness can be rebutted if the applicant . . . can show ‘that the art in any material respect taught away’ from the claimed invention.” *In re Haruna*, 249 F.3d 1327, 58 USPQ2d 1517 (Fed. Cir. 2001). It is respectfully submitted that Vigne, in fact, teaches away from a fiber shaft mutation, insertion or replacement of at least one amino acid in a fiber shaft β -repeat corresponding to the last full β repeat, whereby the fiber has reduced binding to CAR.

In particular, Vigne teaches large deletions or substitutions involving all or most of the Ad5 fiber shaft protein. For example, Vigne teaches viruses having modified Ad5 fibers in which large portions of the fiber shaft (*i.e.*, repeats 4-16 or repeats 4-19, termed viruses “vBS1” and “vBS2”, respectively) are deleted, but the native last full repeat is left intact. Alternatively, Vigne a substitution of the entire Ad5 fiber shaft with the fiber shaft of Ad3 (termed “vB11”). Vigne teaches that viral productivity was reduced in each case for viruses harboring these fiber shaft alterations and suggests that the observed reduction in productivity is likely due to an inability of the modified fibers to interact efficiently with its cellular receptor. However, reduced binding to CAR appears to have only been demonstrated for the vBS1 deletion mutant. Assuming, *arguendo*, that CAR binding was reduced in all of the mutants, the skilled artisan

would conclude that the region responsible for reducing CAR binding would likely be within the region of the Ad5 fiber shaft protein removed or replaced common to all of the mutants (i.e., repeats 4-16).

Indeed, Vigne meets the standard established by the Federal Circuit for teaching away. Specifically, the Court found that “[a] reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant.” *In re Gurley* 27 F.3d 551, 553 (Fed. Cir. 1994). In view of Vigne, one of skill in the art would conclude that CAR binding may be reduced by deletion or replacement of at least repeats 4-16 (See, M.P.E.P. §2145(X)(D)). Thus, the skilled artisan would not consider the last full repeat of the Ad5 fiber shaft protein a viable candidate for a modification to produce a modified fiber having reduced CAR binding. Therefore, the reference teaches away, since the impression left to the skilled artisan is that modification or deletion of regions of the fiber shaft protein including repeats 4-16 are required to reduce binding to CAR. *In re Caldwell*, 319 F.2d 254, 256, 138 USPQ 243, 245 (CCPA 1963).

Thus, it is respectfully submitted that, because Vigne teaches away from a modification of the last full repeat of the fiber shaft protein, the skilled artisan would not be motivated to combine such a fiber shaft modification with a further modification to the fiber knob, as taught in Wickham, nor would the skilled artisan have a reasonable expectation of achieving an adenovirus particle as presently claimed.

It is axiomatic that one cannot simply use Applicants’ disclosure as a “blueprint” to reconstruct, by hindsight, Applicants’ claim. See, e.g., *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 227 USPQ 543 (Fed. Cir. 1985). Because there is neither the suggestion nor expectation of success that can be found in the cited art, no *prima facie* case of obviousness has been established.

Based on the above, it is respectfully submitted that because Vigne teaches away from required claim elements, one of skill in the art would not have had a reasonable expectation of success in achieving the present adenovirus particles and thus, would not have been motivated to combine the references. Accordingly, it is respectfully submitted that no *prima facie* case for

obviousness exists. For these reasons, Applicants respectfully request that this rejection be withdrawn.

Claims 58 and 69-71 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Vigne *et al.*, (supra) in view of Hallenbeck *et al.* (US Patent Appln. Pub. No. 2002/0137213). Applicants traverse the rejection as it applies to the pending claims, for at least the reasons given below.

The Office Action alleges that that Vigne teaches “targeted adenovirus vectors for delivery of heterologous genes, wherein modifications of the internal sites of the adenovirus fiber protein that include short targeting peptides fused to the C-terminus of the fiber protein, or the fiber HI loop (knob) target the modified adenoparticles to specific cell types,” citing the title and abstract (Office Action at p. 5). The Action further alleges that Vigne teaches that the fiber protein may be modified to have a shorter shaft or may be replaced with the shaft of another serotype, but acknowledges that Vigne does not specifically describe the K01 fiber knot mutation. The Action then supplies Hallenbeck in an attempt to cure the deficiencies identified in the primary reference. However, Applicants respectfully submit that the references alone or in combination do not teach all of the elements of the present claims. It is further submitted the references provide no motivation to combine nor would the skilled artisan have had a reasonable expectation of success in achieving an adenovirus particle of the present claims because Vigne teaches away from adenovirus particles having the recited fiber shaft modification.

It is respectfully submitted the Examiner has not met the standard under 35 U.S.C. §103 for establishing a *prima facie* case of obviousness because cited art does not teach all of the elements of the present claims. As discussed above, claim 58 expressly recites that “the modification is a mutation, insertion or replacement of at least one amino acid in a fiber shaft β -repeat corresponding to the last full β repeat, whereby binding of the fiber or of a viral particle containing such fiber to the Coxsackie-Adenovirus Receptor (CAR) is reduced compared to the unmodified fiber.” Such a modification of the last full repeat is not taught by Vigne. Hallenbeck cannot cure this deficiency because Hallenbeck is silent with regard to modifications to the last full repeat of the fiber shaft protein.

Moreover, the arguments presented above regarding the Vigne's teaching away from a modification of the last full repeat of the fiber shaft protein apply equally and are incorporated here. Thus, the skilled artisan would not be motivated to combine such a fiber shaft modification with a further modification to the fiber knob, as taught in Hallenbeck, nor would the skilled artisan have a reasonable expectation of achieving an adenovirus particle as presently claimed.

It is axiomatic that one cannot simply use Applicants' disclosure as a "blueprint" to reconstruct, by hindsight, Applicants' claim. See, e.g., *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 227 USPQ 543 (Fed. Cir. 1985). Because there is neither the suggestion nor expectation of success that can be found in the cited art, no *prima facie* case of obviousness has been established.

Based on the above, it is respectfully submitted that because Vigne teaches away from required claim elements, one of skill in the art would not have had a reasonable expectation of success in achieving the present adenovirus particles and thus, would not have been motivated to combine the references. Accordingly, it is respectfully submitted that no *prima facie* case for obviousness exists. For these reasons, Applicants respectfully request that this rejection be withdrawn.

In re Application of:
Nemerow et al.
Application No.: 10/560,250
Filed: June 22, 2006
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PATENT
Attorney Docket No.: SCRI1870-1

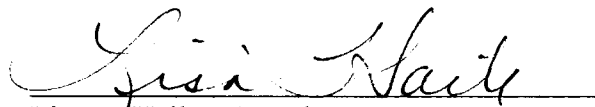
Conclusion

In view of the foregoing amendments and the remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this case.

The Commissioner is hereby authorized to charge the amount of \$180.00 for the Information Disclosure Statement fee to Deposit Account No. 07-1896. No other fee is deemed necessary in connection with the filing of this Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of any such fee, or credit any overpayment, to Deposit Account No. 07-1896.

Respectfully submitted,

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Lisa A. Haile, J.D., Ph.D.
Registration No.: 38,347
Telephone: (858) 677-1456
Facsimile: (858) 677-1465

DLA PIPER US LLP
4365 Executive Drive, Suite 1100
San Diego, California 92121-2133
USPTO CUSTOMER NO.: 28213